

Community-Acquired Methicillin-Resistant *Staphylococcus aureus* Infections in Children

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Community-Acquired Methicillin-Resistant *Staphylococcus aureus* Infections in Children

<u>Authors</u>	<u>Year</u>	<u>Location</u>	<u>Age</u>	<u>Site</u>	Clindamycin <u>Susceptible</u>
Hamoridi et al	1983	OH	6 children outpatients	Skin or wound infections	Yes
Chartrand	1988 Abstract	NE	8 children 2-19y (13 episodes)	deep soft tissue abscess (7) wound infection (5)	NS
Rathore et al	1989	MO	8 y 10 mon	Osteomyelitis Bacteremia	Yes Yes
Gwynne-Jones et al	1999	NZ	25 children	22 superficial 4 deep (3 osteomyelitis)	Most
Gorak et al	1999	HI	17 y 3 y 10 mon 17 y	facial abscess arm abscess lung abscess breast abscess	NS

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<u>Authors</u>	<u>Year</u>	<u>Location</u>	<u>Age</u>	<u>Site</u>	<u>Clindamycin Susceptible</u>
Shahim et al	1999	Toronto	2 .5 y	sepsis (PE tubes)	Yes
Hunt et al (MMWR)	1999	MN	7 y	septic arthritis pneumonia/empyema	Yes
		ND	16 mon	severe sepsis	Yes
		MN	13 y	necrotizing pneumonia	Yes
		ND	12 mon	necrotizing pneumonia	Yes

Community Acquired MRSA in Children

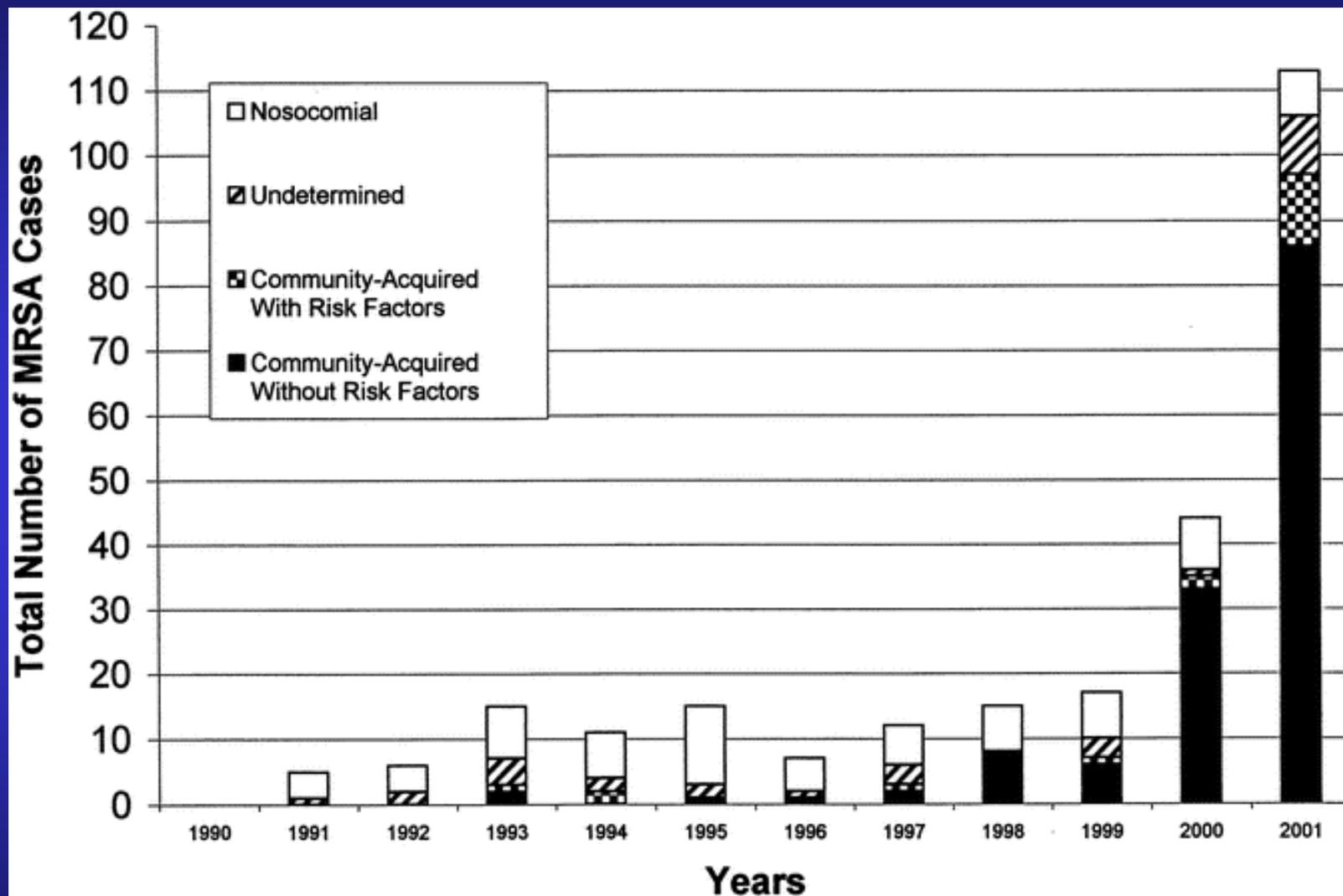
- University of Chicago Children's Hospital
- For 1988-90 8 of 52 MRSA isolates community acquired vs. 35/52 for 1993-95
- Clinical syndromes for MRSA or MSSA infections were similar
- Community-acquired MRSA isolates were more likely to be susceptible to other antibiotics (especially TMP-SMX or clindamycin) than nosocomial MRSA isolates.

Herold et al. JAMA 1998

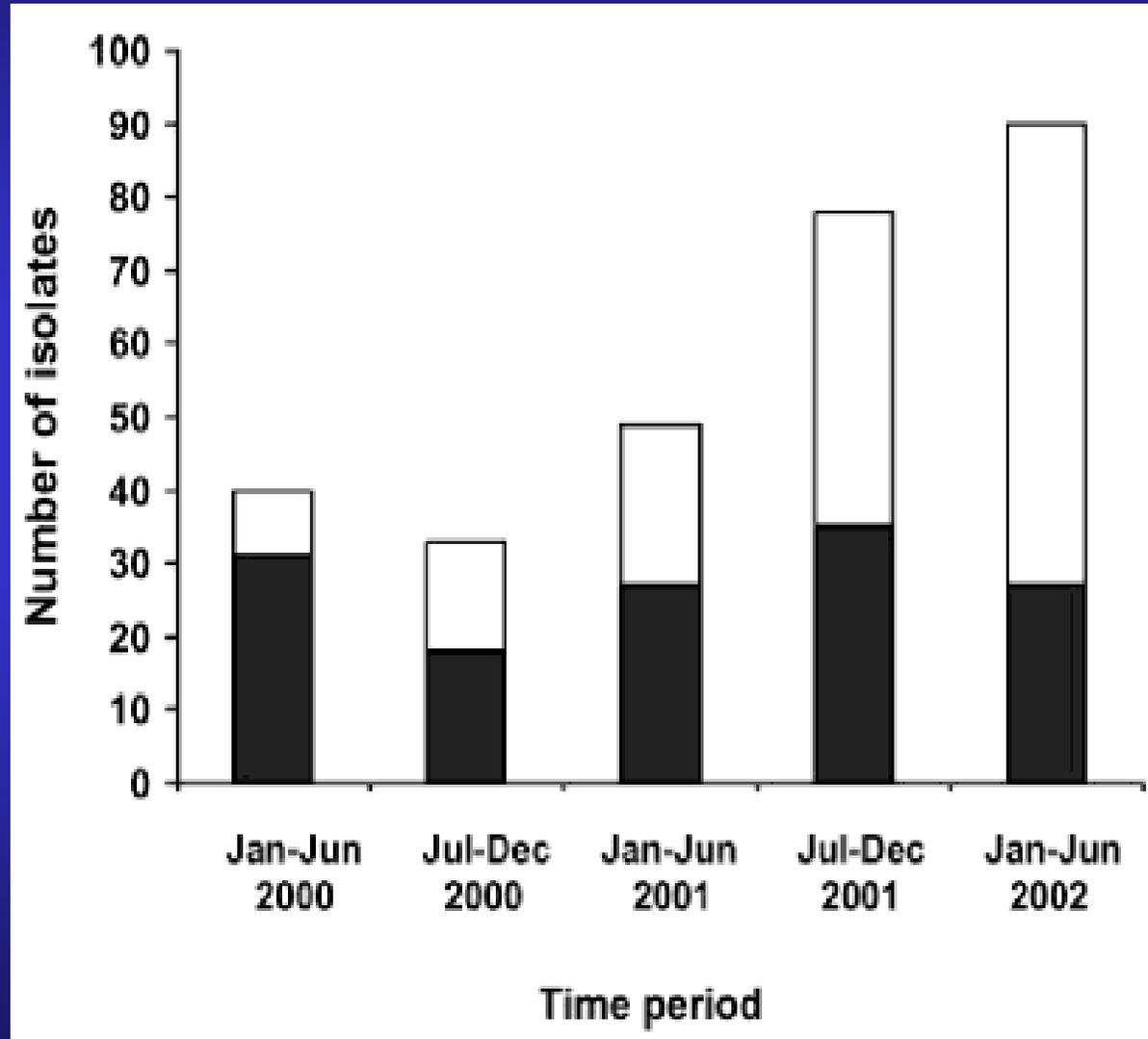
Community-acquired MRSA Infections in South Texas Children

- Of 128 children with MRSA infections, 60 (47%) were community-acquired (CA)
- Proportion CA increased from 12% in 1990 to 80% in 2000
- Soft tissue infections accounted for 91% of CA-MRSA infections in children without risk factors
- Review of MRSA infections at Driscoll Children's Hospital in Corpus Christi, TX from 10/1/90 – 12/31/2000

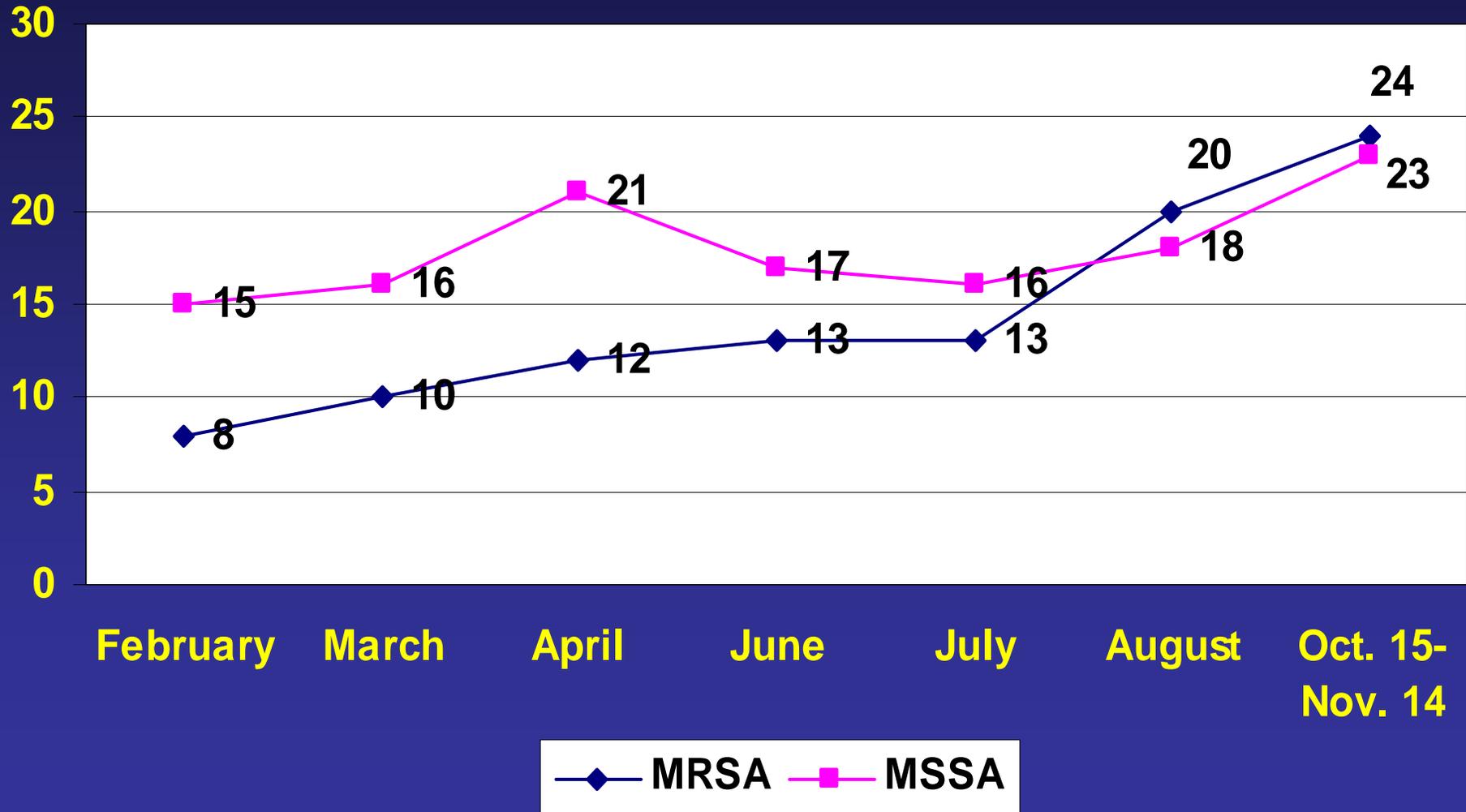
Exponential Increase in CA-MRSA Infections in South Texas Children



Methicillin-resistant *Staphylococcus aureus* isolates cultured from clinical specimens and classified as community-associated (□) or health care-associated (■) at Le Bonheur Children's Medical Center from January 2000 to June 2002.



Number of *Staphylococcus aureus* Isolates Per Study Month and Susceptibility to Methicillin at Texas Children's Hospital, Feb.-Nov. 2000*



*includes both enrolled and non-enrolled, eligible patients

Sattler et al PIDJ 2002

Demographic/clinical characteristics of patients with MRSA/MSSA community acquired infection at Texas Children's Hospital, Feb.-Nov. 2000

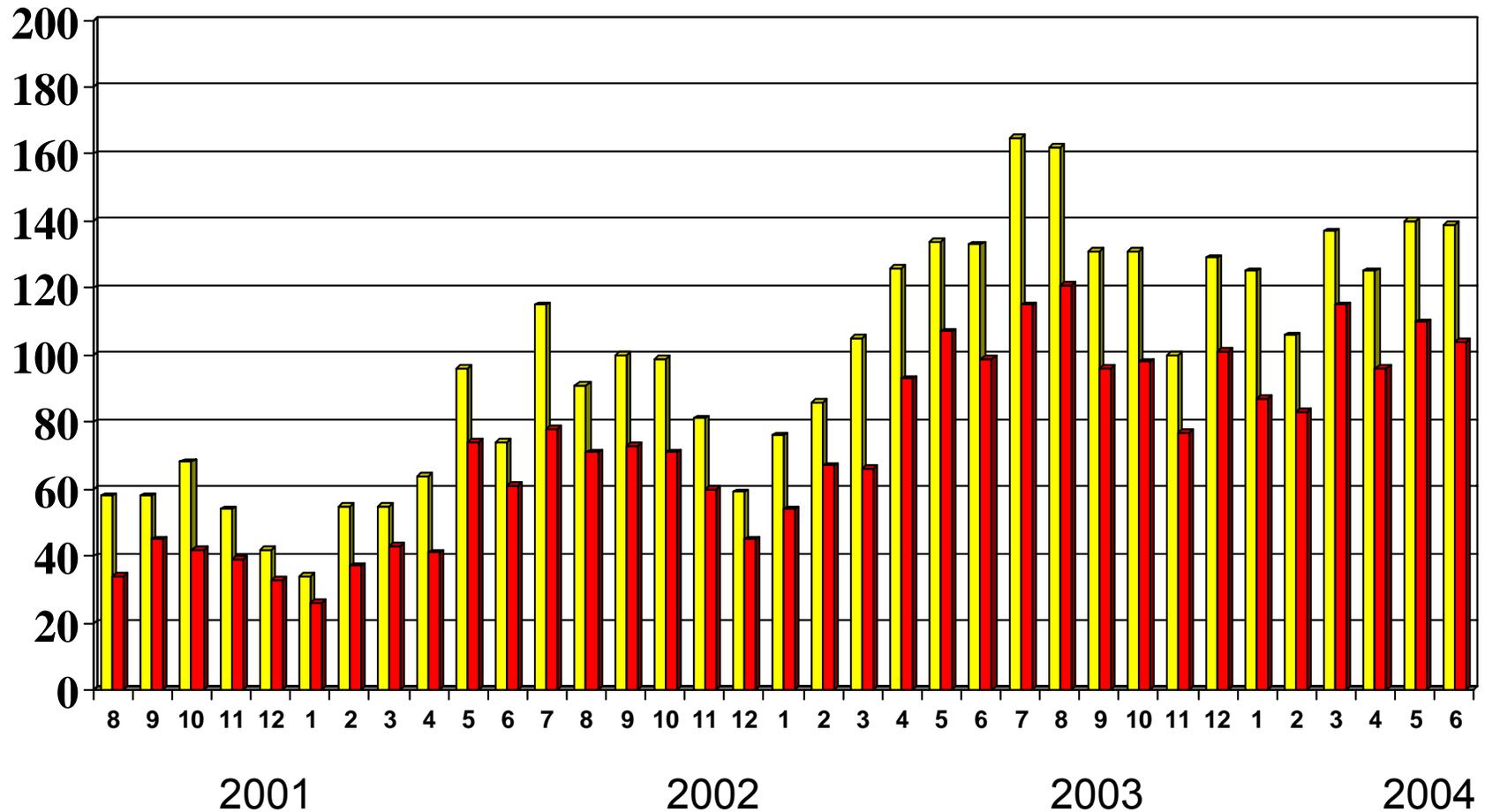
	MRSA (N=64)	MSSA (N=80)	<i>p</i>
<u>Mean age</u> (range)	6.7 years (14 days - 18.3 years)	5.9 years (23 days - 16.8 years)	<i>p</i> = NS
<u>Sex</u> (% males)	50	56	<i>p</i> = NS
<u>Race</u> (%)			
– White	16 (25)	32 (40)	
– Black	31 (48.4)	17 (21.3)	<i>p</i> = 0.0036
– Hispanic	13 (20.3)	28 (35)	
–Other	4 (6.3)	3 (3.8)	
<u>Mean #</u>			
<u>household contacts</u> -	4.5	4.7	<i>p</i> = NS
<u>Health Insurance</u> (%)			
–Commercial/ Mng. Care	34 (53.1)	47 (58.8)	
–Medicaid	23 (35.9)	20 (25)	<i>p</i> = NS

Demographic/clinical characteristics of patients with MRSA/MSSA community acquired infection at Texas Children's Hospital Feb.-Nov. 2000

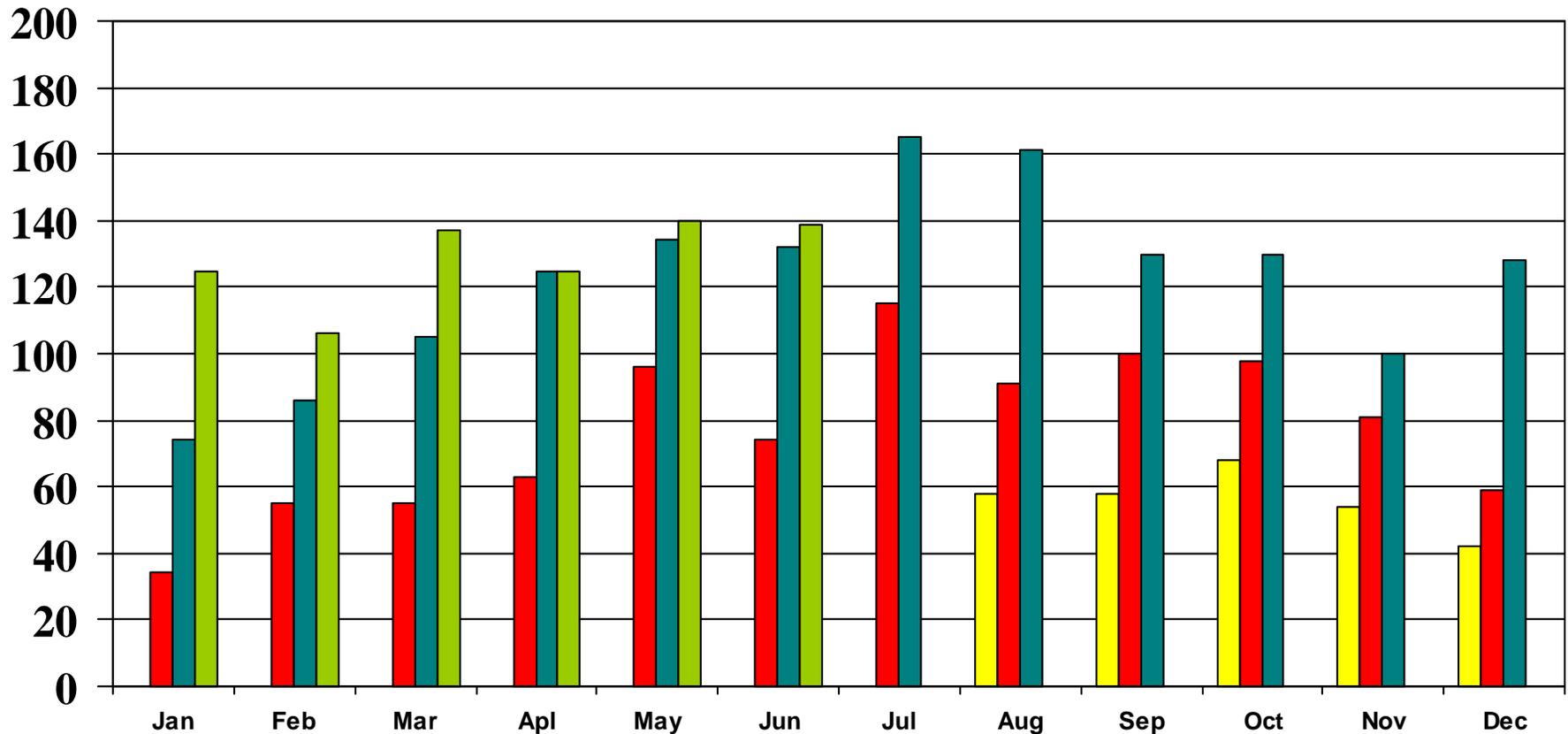
	MRSA (N = 64)	MSSA (N = 80)	<i>p</i>
<u>Inpatients (%)</u>	47 (73.4)	64 (80)	<i>p = NS</i>
<u>Skin/Subcutaneous tissue infections (%)</u>	57 (89.1)	58 (72.5)	
– Superficial skin infections/abscess	36	36	
– Cellulitis	21	22	
<u>Deep-seated infections (%)</u>	7 (10.9)	22 (27.5)	<i>p = 0.02</i>
– Osteomyelitis / septic arthritis	2	11	
– Pneumonia	2	2	
– Pyomyositis	3	1	
– Lymphadenitis	–	3	
– Other	–	5	

Isolation of Community Acquired *S. aureus* at Texas Children's Hospital

■ *S. aureus* ■ MRSA

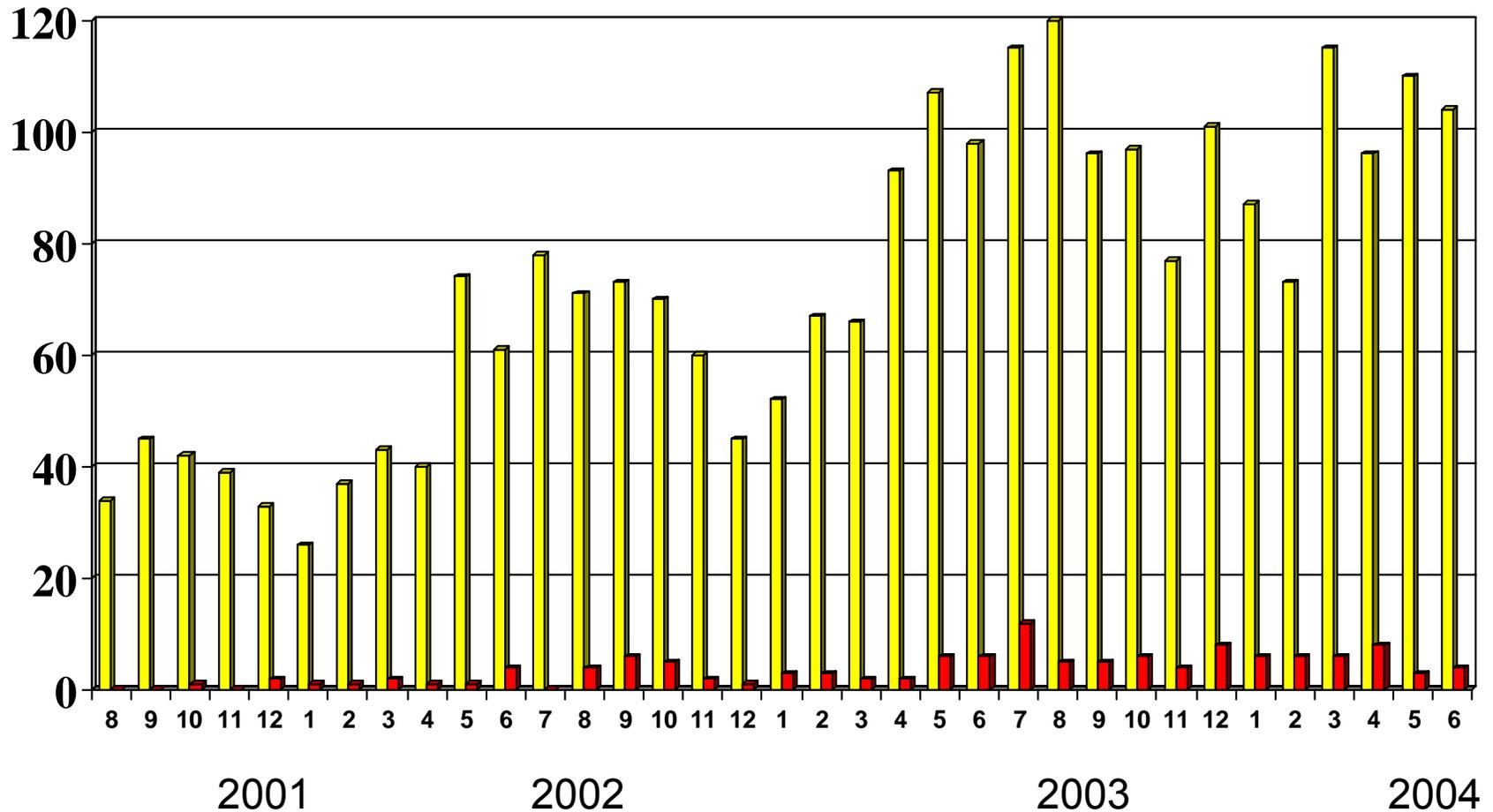


Isolation of Community Acquired *S. aureus* at Texas Children's Hospital

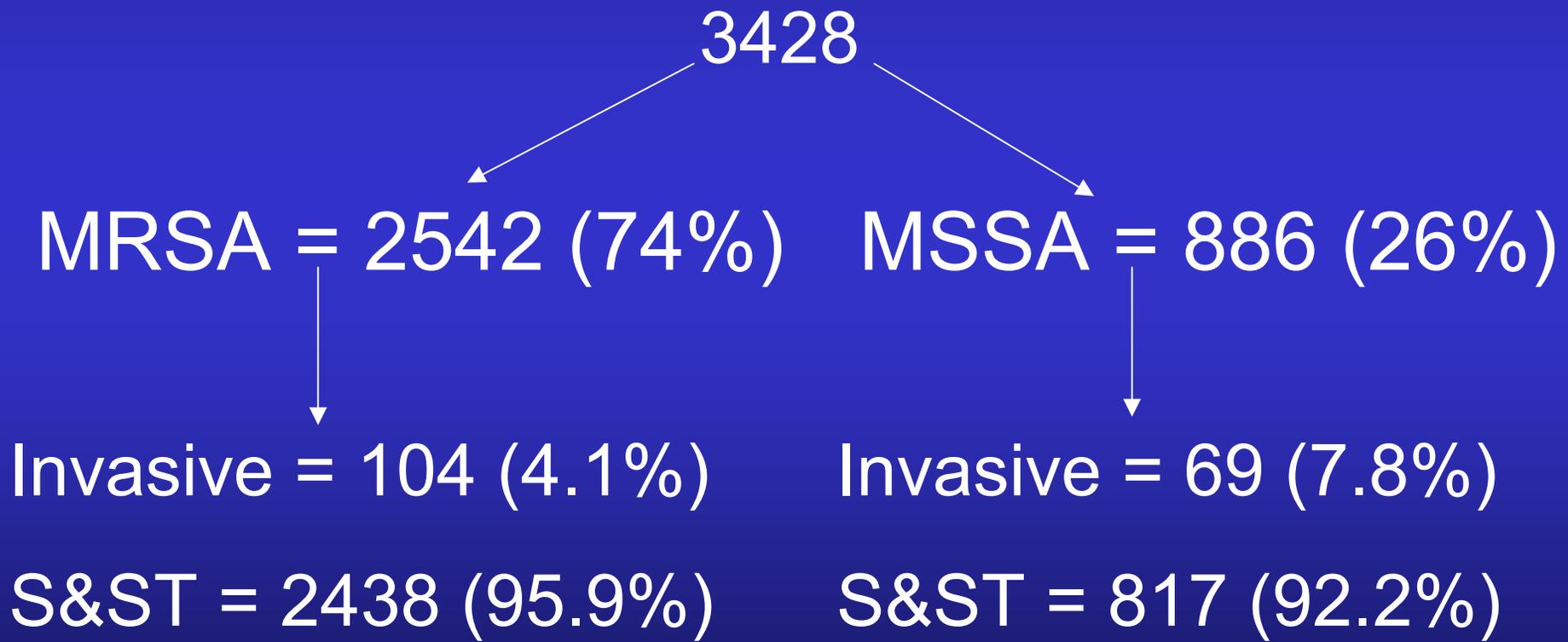


Clindamycin Susceptibility of CA-MRSA at Texas Children's Hospital

■ MRSA **■ Clindamycin R**

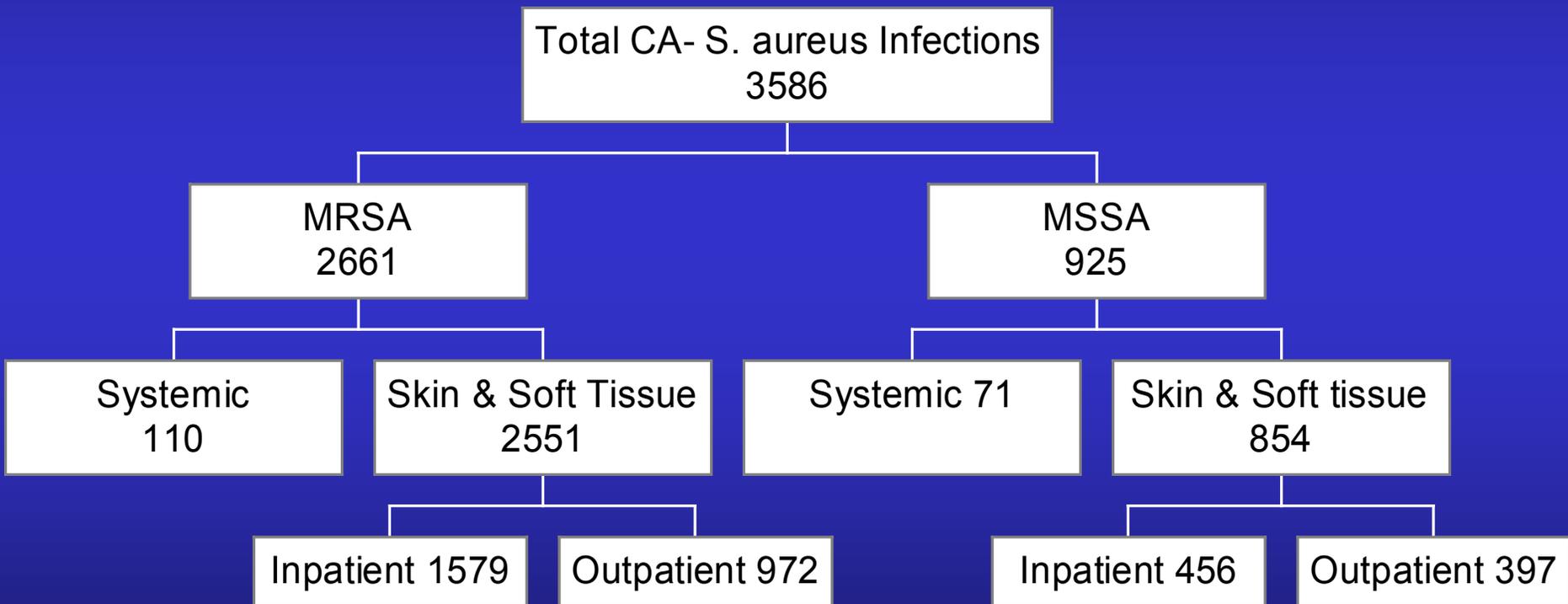


Community Acquired *S. aureus* Texas Children's Hospital August 2001 – June 2004



P < 0.000001

CA-*S. aureus* Infections TCH August 1, 2001 to July 31, 2004



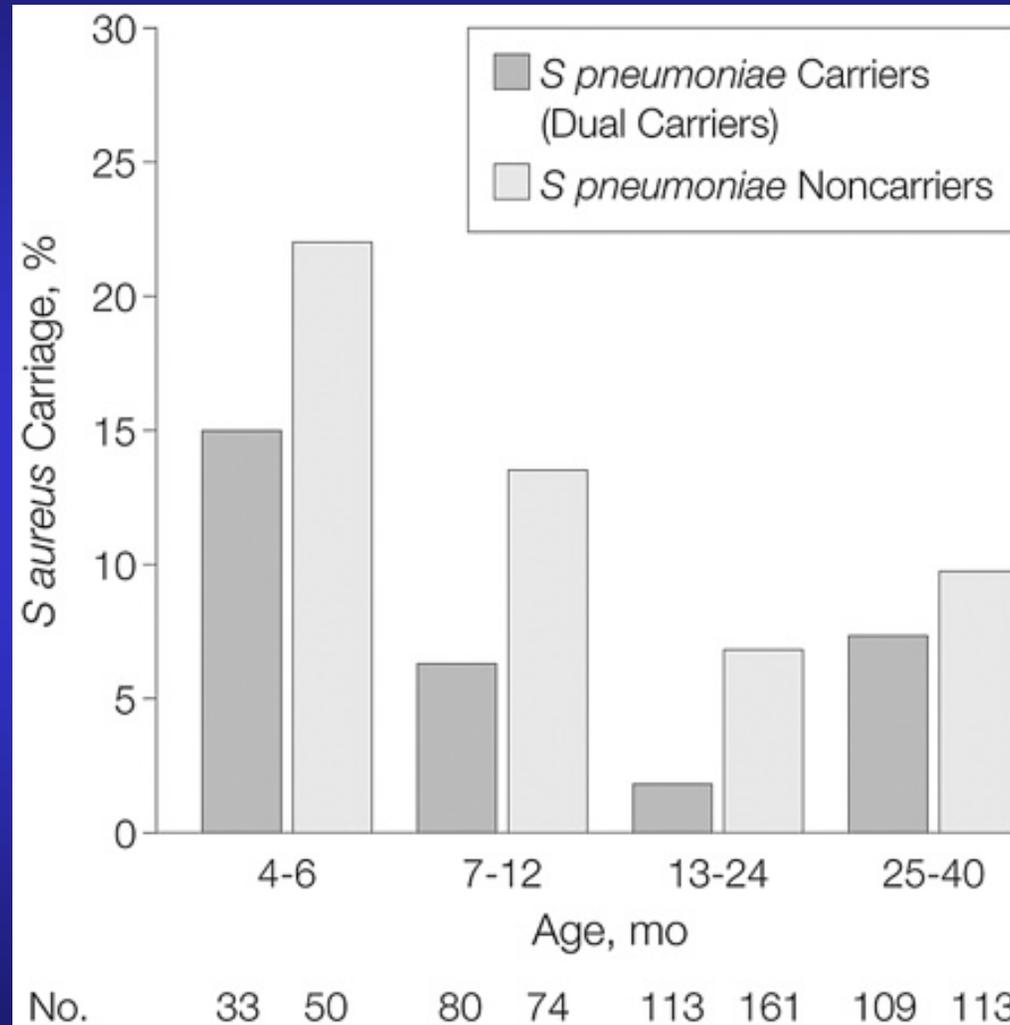
Streptococcus pneumoniae and *Staphylococcus aureus* Colonization in Healthy Children

	<i>S pneumoniae</i> colonisation			Total
	No	Non-vaccine serotypes	Vaccine serotypes	
<i>S aureus</i> colonisation				
No	1570	219	191	1980
Yes	930	129	58	1117
Total	2500	348	249	3097

χ^2 19.63, p value: <0.001.

Negative correlation for co-colonization of *S aureus* and vaccine-type pneumococci (OR 0.68, 0.48–0.94), but not for *S aureus* and non-vaccine serotypes. These findings suggest a natural competition between colonization with vaccine-type pneumococci and *S aureus*.

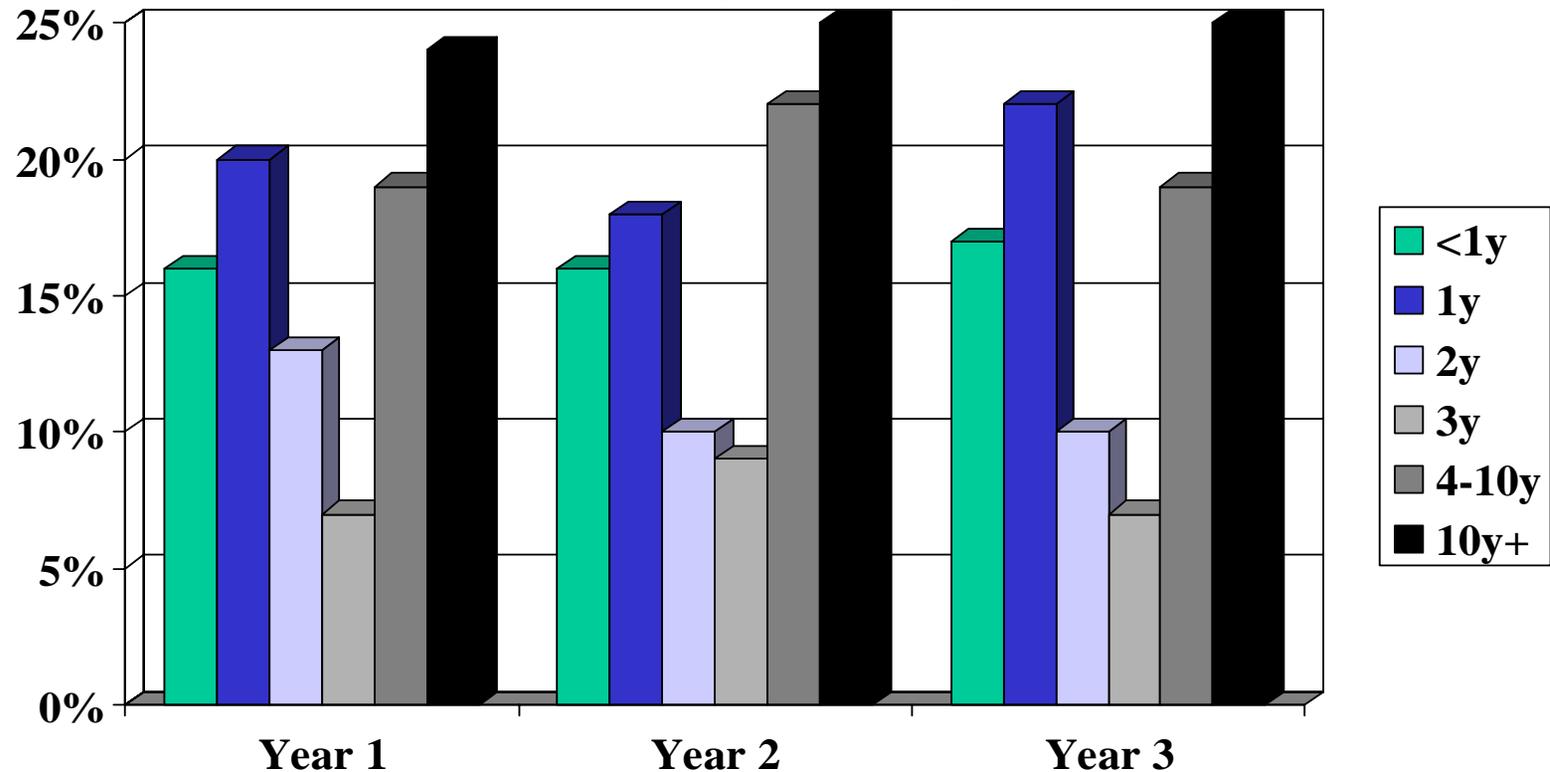
Association Between *Streptococcus pneumoniae* and *Staphylococcus aureus* Stratified by Age Group



Mantel-Haenszel odds ratio, 0.51 (95% confidence interval, 0.29–0.89).

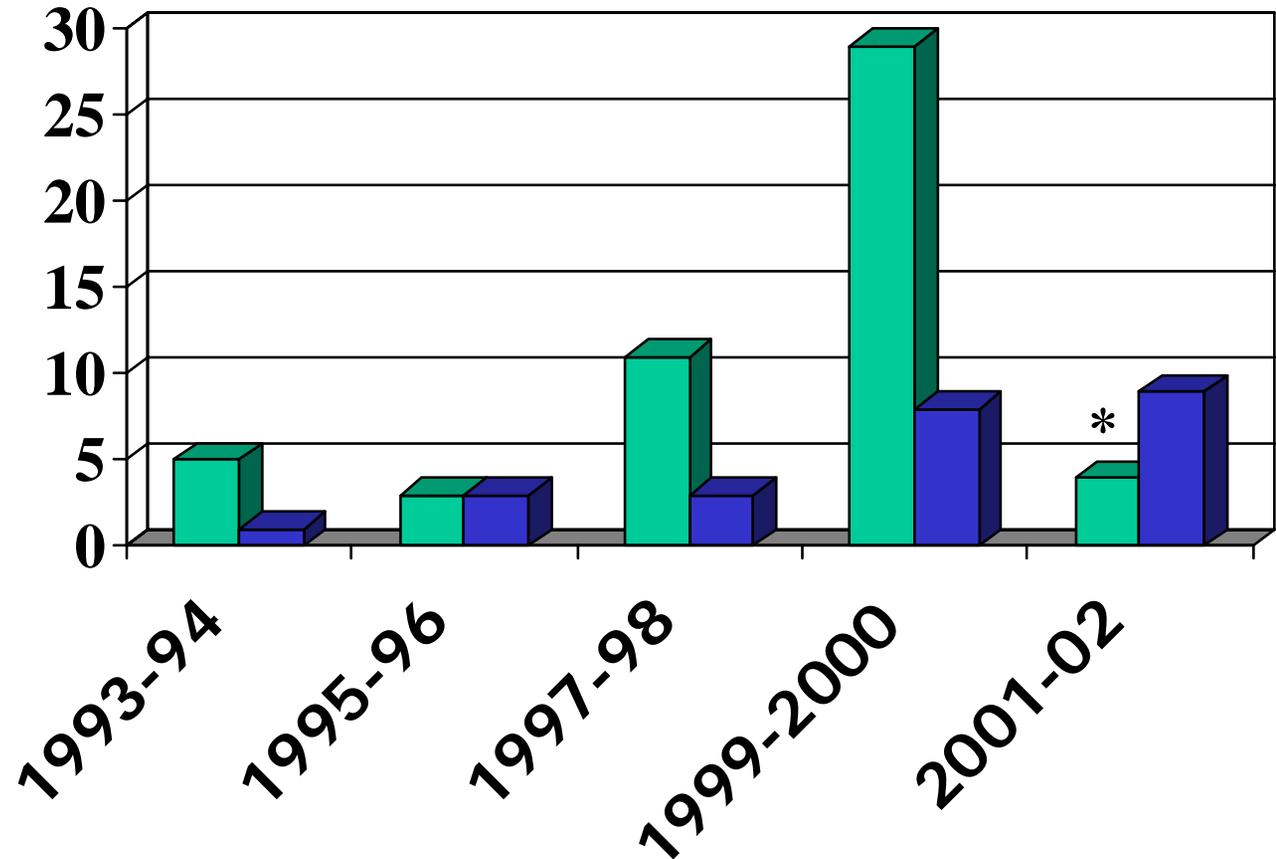
Regev-Yochay et al JAMA 2004;292:716–720

Community-acquired *Staphylococcus aureus* Infections at TCH Starting August 1, 2001



Bacterial Etiology of Pleural Empyema at TCH

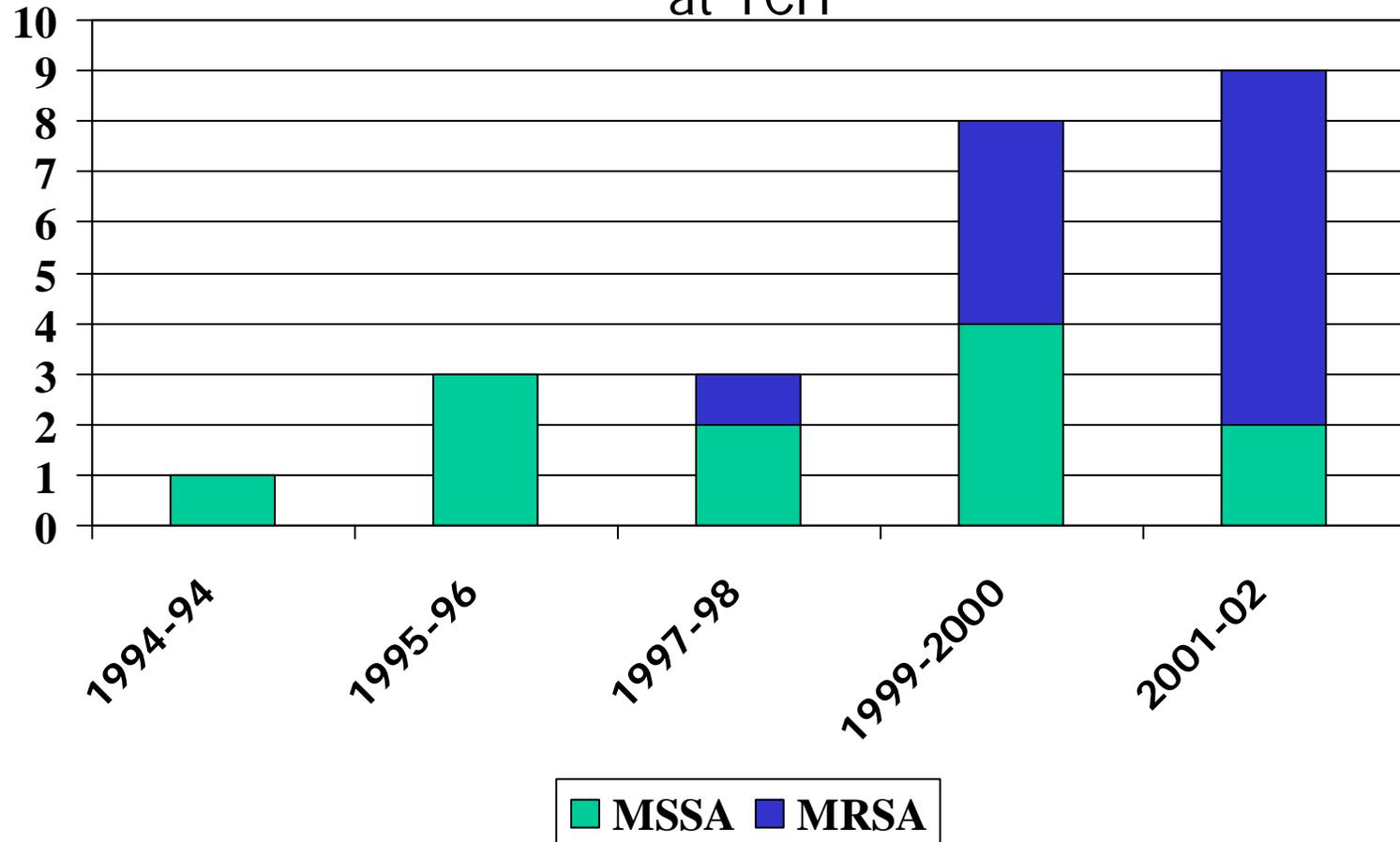
Schultz et al Pediatrics 2004



*p=0.03, 1999-2000 vs 2001-2002



Cases of Empyema Caused by MSSA and MRSA at TCH



Schultz et al Pediatrics 2004

Severe Staphylococcal Infections in the Era of MRSA

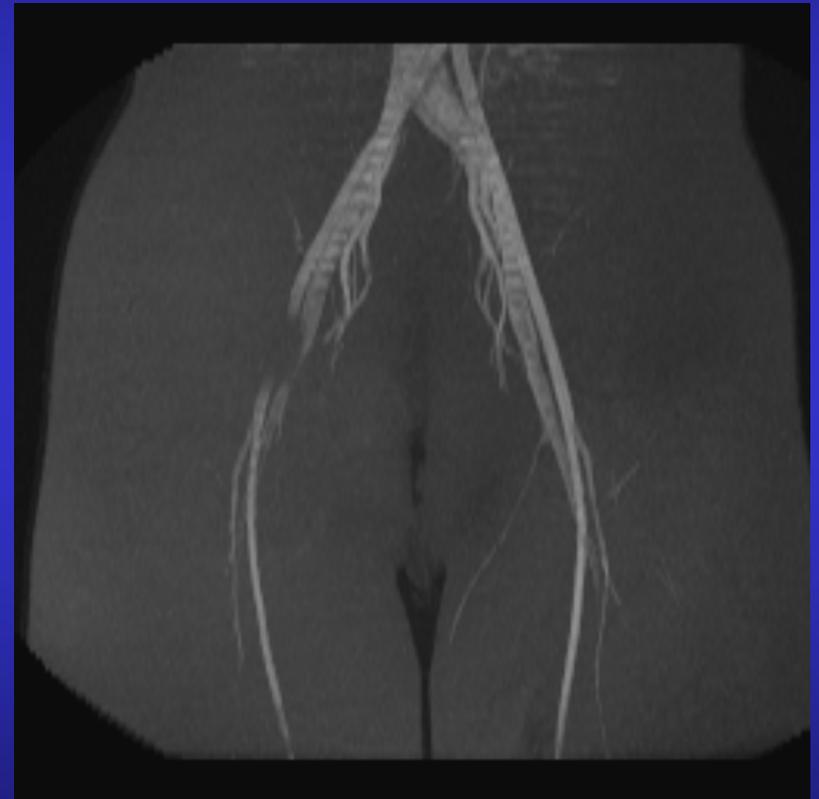
- Between 9-2002 and 11-2003, 153 patients with invasive CA-SA infections were admitted to TCH.
- **15 patients** (9%) with severe CA-SA infections admitted to the PICU were identified.
- 13 (87%) patients had **CA- MRSA**
- 2 patients had **CA-MSSA**
- 13 were male (87%)
- **Mean age** : 12.2 years (1.5-17)
- **Race**: 8 Caucasian; 5 black; 2 Hispanic.
- **Mean weight** : 62.7 kg (14-104)

Severe Staphylococcal Infections in the Era of MRSA

- **Underlying Conditions:** 12 (80%) none; 2 Asthma; 1 history of PDA.
- **History of Trauma:** 9 (60%) had blunt trauma to an extremity which occurred on average 6 days prior to admission.
- **Other diagnosis** on admission: 2 Influenza A; 1 Parainfluenza, 1 HSV.
- 13 patients had **bone and joint** involvement, 8/13 had more than 1 site involved.
- 13 patients had **pulmonary** involvement: Air space disease, septic emboli, pneumonia and empyema, pneumatoceles.

Severe Staphylococcal Infections in the Era of MRSA

- 4/15 patients had **vascular complications:**
- Deep venous thrombosis
- Pseudoaneurysms



Musculoskeletal Infection and DVT

- Few cases in the literature.¹⁻⁴
 - Two of six children with osteomyelitis, DVT and septic pulmonary emboli died.
- Osteomyelitis, septic arthritis, pyomyositis
 - S. aureus* usually 40-80% vs. 90% in DVT cases
- Exotoxins
 - Alpha-toxins act on cell membranes, produce aggregation of platelets, smooth muscle spasm
- Coagulase
 - Interacts with fibrinogen, causes plasma to clot

¹Horvath et al. *J Pediatr* 1971;79:815

²Jupiter et al. *J Pediatr* 1982;101:690

³Walsh and Phillips. *J Pediatr Orthopaed* 2002;22:329

⁴Gorenstein et al. *Pediatr* 2000;106:e87

Severe Staphylococcal Infections in the Era of MRSA

- All Patients were admitted to the ICU
- 3 had leukopenia on admission
- 12 (80%) required pressors.
- Mean Duration of Fever: 11.2 days (0-35)
- Blood cultures were positive in 13 patients.
- Mean duration of bacteremia was 4 days (1-11)
- All with positive D-dimers and FSP
- Mean duration of stay: 17.8 days (1-53)

OUTCOME

- 4 patients died
 - 3 CA-MRSA
 - 1 CA-MSSA
- All four had pulmonary manifestations
- 3/4 had bone and joint involvement
- 3 had leukopenia on admission

Panton-Valentine leukocidin

- The *pvl* gene encodes the Panton-Valentine leukocidin.
- This cytotoxin creates lytic pores in leukocytes.
- The *pvl* gene was significantly more common in our CA-MRSA isolates than the CA-MSSA isolates and was found in over 90% of the CA-MRSA isolates during each study period.
- The *pvl* gene has been linked with superficial infections or community acquired pneumonias characterized by a hemorrhagic necrotizing process and high mortality rates.

Complications in children with musculoskeletal infections caused by community-acquired *Staphylococcus aureus* isolates containing or lacking the *pvl* gene. 2000-2002

Outcome	<i>pvl</i> Positive (n = 33)	<i>pvl</i> Negative (n = 23)	P value
Complications			
Chronic Osteomyelitis at admission	3	0	0.002
Chronic Osteomyelitis noted first on follow-up	3	0	
Deep Venous Thrombosis*	5	0	
Total	11(10)**	0	
Febrile days			
Mean ± SD	4.2 ± 3.6	2.1 ± 2.5	0.017
Median (Range)	4 (0-14)	2 (0-10)	

Community-Acquired Methicillin-Resistant *Staphylococcus aureus* Infections in Children

Implications - Skin or Soft-Tissue Infections

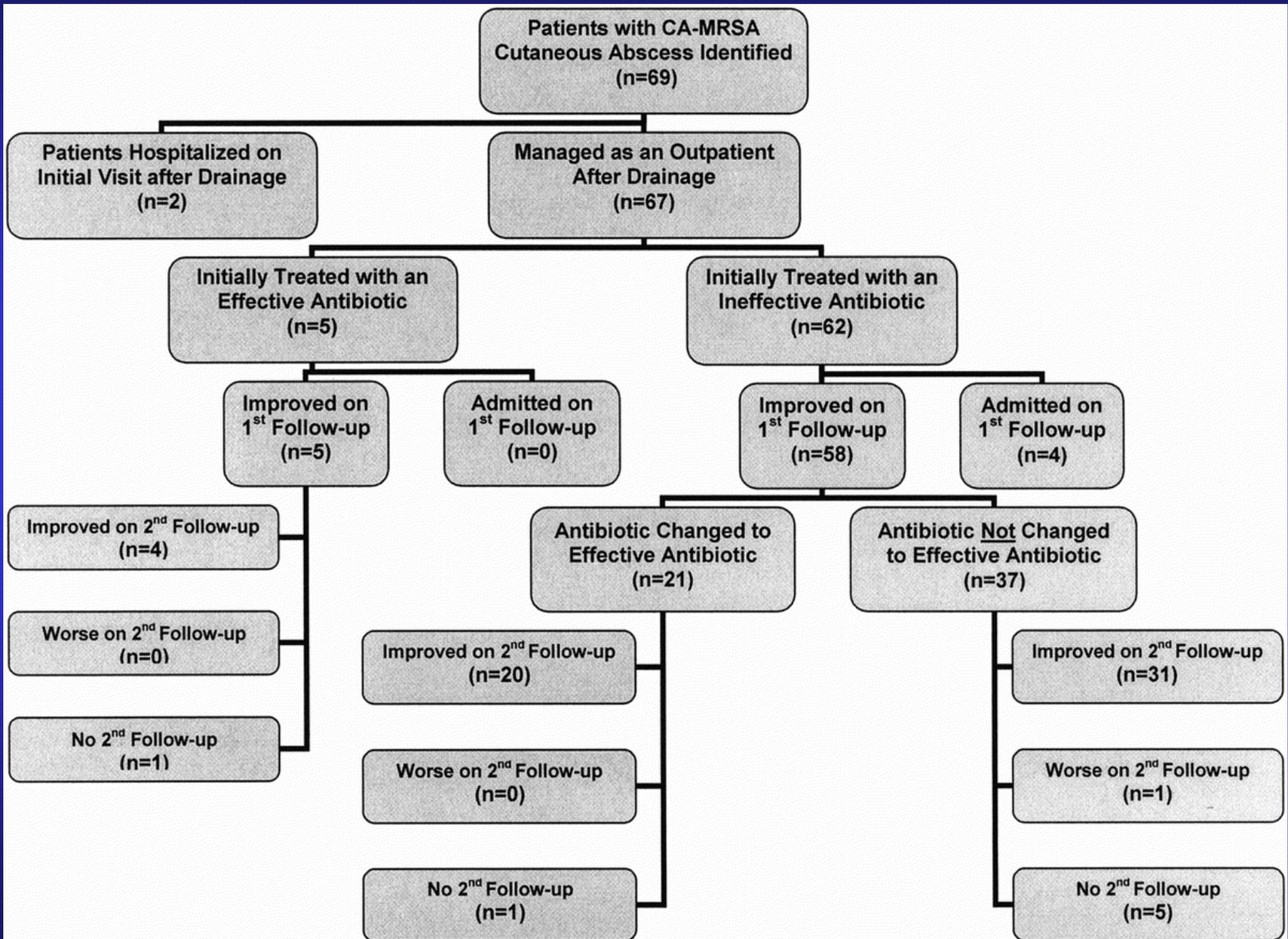
- Minor skin infections or abscesses caused by MRSA in the normal child usually resolve even with β -Lactam antibiotics \pm surgical drainage.
- If cellulitis or abscess is progressing despite conventional oral antibiotics \pm drainage, consider MRSA as possible etiologic agent. Obtain cultures and consider switching antibiotics to clindamycin or TMP/SMX (if GAS not a concern).
- Once CA-MRSA is common, clindamycin or TMP/SMX becomes standard empiric therapy

TABLE 1. Characteristics of subjects

Subjects	69 (except as noted)
Mean age range	4 mo–17 yr; mean 5.5 yr
Male	28 (41)*
Race	
White	4 (6)
African American	45 (65)
Hispanic	20 (29)
Day care	21/62 (34)
Recent hospitalization of family member	12/62 (19)
Health care worker in family	13/62 (21)
Recent visit to institutional care facility (e.g. nursing home)	5/62 (10)
Asthma	13 (19)
Eczema	3 (4)
History of prior cutaneous abscess	8 (12)
Abscess location	
Buttock	20 (29)
Thigh	12 (17)
Groin	6 (9)
Perirectum	4 (6)
Other	27 (39)
Incision and drainage	62 (90)
Manual expression	4 (6)
Spontaneous drainage	3 (4)
Abscess packed	45 (65)
iv antibiotic during initial evaluation (all beta-lactams)	22 (32)

* Numbers in parentheses, percent.

Management of C-MRSA Cutaneous Abscesses-Dallas



Management of CA-MRSA Cutaneous Abscesses

- 4 outpatients initially treated with ineffective antibiotics were admitted at 1st follow-up
- A significant predictor of hospitalization on the 1st f/up was having an infected area > 5 cm in diameter at the initial visit (33% were later hospitalized) vs. none with a diameter ≤ 5 cm; $P=0.004$
- Ineffective initial antibiotic was not predictive of subsequent hospitalization

Community-Acquired Methicillin-Resistant *Staphylococcus aureus* Infections in Children

Implications - Severe or Life-Threatening Infections

In areas in which MRSA accounts for $\geq 10\%$ (?) of community-acquired *S. aureus* isolates, clinicians should consider modifications for initial empiric therapy of severe infections for which *S. aureus* is among the potential etiologic agents which include:

- (1) Septic shock (Vancomycin + rifampin + nafcillin + gentamicin)
- (2) Osteomyelitis/septic arthritis (Vancomycin or Clindamycin*)
- (3) Severe cellulitis requiring hospitalization or worsening on standard treatment (Clindamycin or Vancomycin)
- (4) Critically ill child with pneumonia*/empyema (Vancomycin or Clindamycin)

*** Need to know the clindamycin susceptibility of CA-MRSA isolates in your area**

Clindamycin Treatment of Invasive Community-Acquired *Staphylococcus aureus* Infections

- Compared the outcome of therapy for CA-MRSA vs. CA-MSSA infections in children treated with clindamycin, vancomycin or β -lactam antibiotics
- Records at TCH from February 2000 – November 2000 and August 2001 – July 2002 reviewed for CA-*S. aureus* invasive infection
- *S. aureus* isolates tested by K - B for “D”- zone

Martinez et al. PIDJ 2003

TABLE 1. Demographic and clinical characteristics of patients with community-acquired MRSA and MSSA invasive infections at Texas Children's Hospital

Variable	MRSA (n = 46)	MSSA (n = 53)	P
Age (mean ± SD) in yr	5.0 ± 4.7	7.2 ± 5.8	
Median (range)	3.5 (2 mo–18.6 yr)	4.8 (3 mo–19.8 yr)	NS
Gender male	28	28	NS
Race			
African-American	24	21	0.0001
White	11	5	
Hispanic	11	23	
Asian		2	
Other		2	
Underlying conditions			
Asthma	2	2	NS
Chronic skin illness*	3	3	
Malignancy†	1	1	
Autoimmune diseases		1	
Other	2	1	
Surgical interventions			
Yes	40 (87.0%)	38 (75.0%)	NS
No	6 (13.0%)	15 (25.0%)	

* Eczema (5 of 6)

† Had *Staphylococcus aureus* infection at clinical presentation before diagnosis of the malignancy.

TABLE 2. Site of infection in patients with community-acquired MRSA and MSSA invasive infections

Site of Infection	MRSA (<i>n</i> = 46)	MSSA (<i>n</i> = 53)	<i>P</i>
Bacteremia	3	6	
Osteomyelitis*	14 (9)†	14 (5)	
Septic arthritis	5 (2)	7 (4)	
Complicated pneumonia‡	11 (1)	3 (1)	0.001
Lymphadenitis	7	14	
Deep abscesses§	1	2	
Pyomyositis	2 (1)	4 (2)	
Mastoiditis		1	
Bursitis	2	1	

* Five patients also had myositis as documented by MRI studies.

† Numbers in parentheses, number of patients with positive blood cultures.

‡ All but one patient had complicated pneumonia: empyema (11); lung abscess (2). In one patient the diagnosis was established by sputum culture.

§ Cerebral, paraspinous, psoas.

Antibiotic susceptibility of MRSA and MSSA isolates from children with invasive *S. aureus* infections. Martinez et al. PIDJ 2003

	MRSA (n = 46)		MSSA (n = 53)		P value
	R n (%)	S n (%)	R n (%)	S n (%)	
Erythromycin	38 (83)	8 (17)	9 (17)	44 (83)	0.0001
Clindamycin	2 (4)	44 (96)	0 (0)	53 (100)	NS
TMP/SMX	0 (0)	46 (100)	1 (2)	52 (98)	
Gentamicin	0 (0)	46 (100)	0 (0)	53 (100)	
Vancomycin	0 (0)	46 (100)	0 (0)	53 (100)	
Penicillin	46 (100)	0 (0)	50 (94)	3 (6.0)	

TABLE 3. Antibiotics used for the treatment of CA-MRSA and CA-MSSA invasive infections

Antibiotics	MRSA (<i>n</i> = 46)		MSSA (<i>n</i> = 52)	
	Initial	Final	Initial	Final
Clindamycin*	20	39	18	24
Nafcillin	5	0	16	18
Vancomycin†	18	6	15	0
Other β -lactam antibiotics‡	3	0	3	9
TMP-SMX	0	1	0	1

* In 9 patients combined with gentamicin or cefotaxime; 4 in the MRSA and 5 in the MSSA.

† Usually combined with nafcillin or other β -lactams.

‡ Cephalosporins, ticarcillin/clavulanic acid.

TABLE 5. Hospital course and outcome of children with invasive CA-MRSA and CA-MSSA infection

Outcome	MRSA (<i>n</i> = 46)	MSSA (<i>n</i> = 53)	<i>P</i>
Cure/improvement	45	52	NS
Death	1	1	
Febrile days			0.07
Mean \pm SD	3.93 \pm 4.12	1.81 \pm 1.69	
Median	3 (0–14)*	2 (0–6)	
Hospital days			0.005
Mean \pm SD	12.02 \pm 7.64	9.02 \pm 8.54	
Median	9 (3–37)	7 (0–44)	
PICU days	<i>n</i> = 8	<i>n</i> = 3	0.49
Mean \pm SD	6.50 \pm 4.75	9 \pm 4.36	
Median	9 (1–15)	7 (6–14)	
Days of BC+	<i>n</i> = 16	<i>n</i> = 18	0.04
Mean \pm SD	3.38 \pm 2.45	1.50 \pm 1.04	
Median	2 (1–11)	1 (1–4)	
Days of BC+ [†]	<i>n</i> = 15	<i>n</i> = 18	0.084
Mean \pm SD	2.87 \pm 2.45	1.50 \pm 1.04	
Median	1 (1–8)	1 (1–4)	

[†] Excluding one patient with 11 days of positive cultures (see text).
* Numbers in parentheses, range.
PICU, pediatric intensive care unit; BC+, blood culture-positive.

Clindamycin Treatment of Invasive Community - Acquired *Staphylococcus aureus* Infections

Outcome

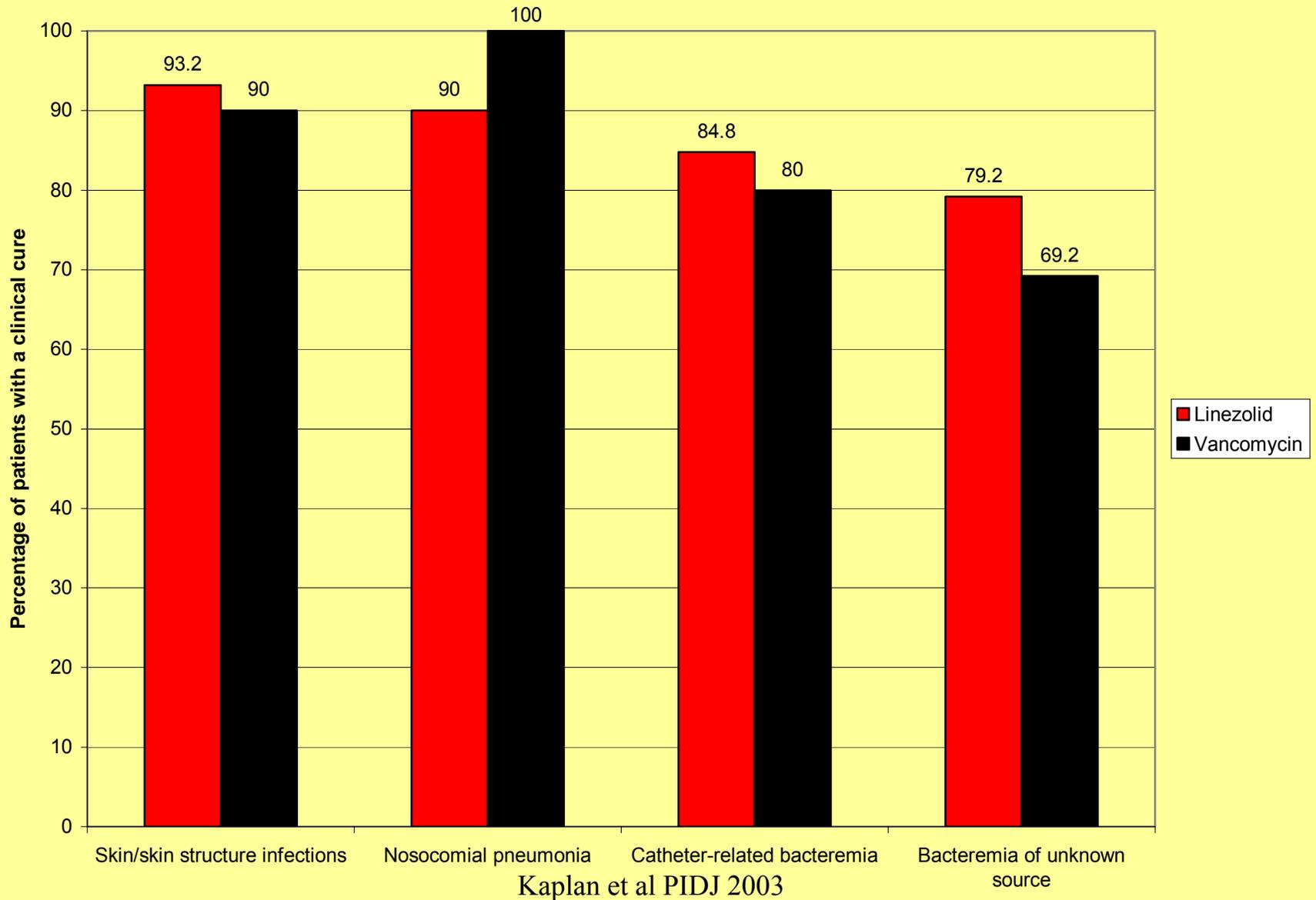
- All but one child with MRSA infection was cured with clindamycin. One MRSA child with undrained pyomyositis and septic thrombophlebitis was switched from clindamycin to vancomycin
- Vancomycin was effective in all 6 MRSA patients
- All MSSA infected patients were cured except one who died prior to treatment

Martinez et al PIDJ 2003

Oxazolidinones - Linezolid

- Bind to 50S ribosome to inhibit protein synthesis but at a different site than for aminoglycosides, macrolides or clindamycin
- Bacteriostatic for *S. aureus* and *Enterococcus* spp (including MRSA and VRE); bactericidal for *S. pneumoniae* (including PRP)
- Active against *Nocardia* spp and certain atypical mycobacteria
- Resistance in VRE and one MRSA isolate has developed 2° to amino acid change of 50S ribosomal unit

Linezolid Versus Vancomycin in Hospitalized Children



Daptomycin

- Most rapidly bactericidal agent in vitro against MRSA
- Approved for use in US for skin and soft tissue infections
- CPK levels should be monitored weekly since drug associated with muscle pain and weakness
- No PK or safety studies in children

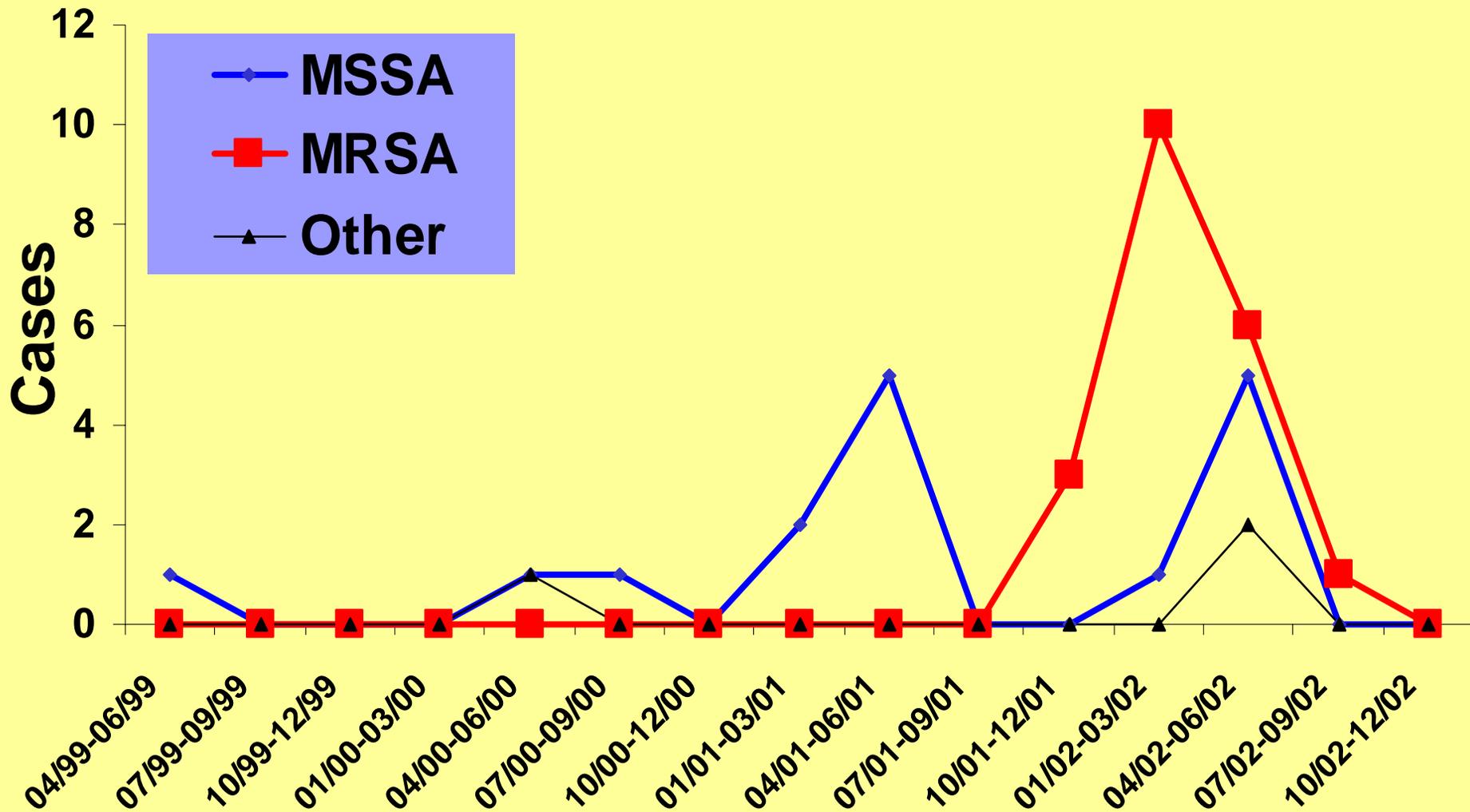
Community-Acquired Methicillin-Resistant *Staphylococcus aureus* Infections in Children

- Recurrent skin infections are common and even more frequent in children with eczema
- Infections in more than one family member is common
- Outbreaks among students in contact sports such as football and wrestling are common

Prevention of Recurrent CA-MRSA Infections

- Routine Hygiene-cut fingernails short; daily changes of sleep wear, underwear, towels and wash cloth
- Mupiricin to anterior nares 2 or 3 times daily for 3-4 weeks (14% of US isolates resistant)
- Bathe in water with regular Clorox® (1 teaspoon/gallon) twice a week for 15 min

Sodium Hypochlorite - MRSA



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Sports

SECTION C

Wednesday, October 15, 2003

Sportsline

Baseball/AL Championship Series Coverage, 4C

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NL Championship Series Coverage, 5C

Florida at Chicago

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N.Y. Islanders 2, Atlanta 2

Edmonton at Calgary

Staph infections surface in sports

A bacteria that flourishes in athletic settings and is resistant to most antibiotics is causing concern, 1A, 12C

Sports teams, pro and amateur, warned of skin infection

By Gary Mihoces
USA TODAY

Concern is growing within the sports world and medical community over a bacterial skin infection that is resistant to usual antibiotics and flourishes in athletic environments.

Recent cases on high school, college and pro football teams have been reported from Wisconsin to California to Texas to Florida. Those hospitalized included Miami Dolphins star linebacker Junior Seau, according to Florida newspapers.

A report by the national Centers for Disease Control and Prevention cited cases on a Colorado fencing team and an Indiana wrestling team.

According to the CDC, the bacteria is spread in ways that come with the territory in sports, including contact with infected persons or by contact with shared towels or equipment that carry the bacteria. The infection develops in routine cuts and scrapes.

"This is more of a beginning than a blip," says Bill Wucherer, health officer for Franklin, Wis.,

where eight high school football players were infected.

On Monday the National Collegiate Athletic Association issued an "alert on skin infections" to schools. The National Federation of State High School Associations says it will send a similar alert this week to high school sports bodies.

In August, the medical and training staffs of every National Football League club were sent copies of a CDC report about infections in sports related to the bacteria called methicillin-resistant staphylococcus au-

reus (MRSA).

"It's up to the physicians to be aware of it and respect the fact it could happen," says Elliot Pellman, team physician of the NFL's New York Jets.

Cases had been associated with patients in hospitals.

"Now we're seeing it emerge in settings where people have little or no contact with health care and are generally healthy. . . . Sports teams are just the last couple of years," says Jeff Hageman, an epidemiologist with the CDC in Atlanta.

The CDC links the trend to

the growing increase in resistance to antibiotics, but while MRSA is resistant to commonly used penicillin-related antibiotics, the CDC says the infections are treatable with other antibiotics.

Because it is not a typical staph infection, MRSA must be identified through tests of culture samples. Wounds accompanied by fever, swelling, redness and oozing are suspect as are boils.

► **How sports teams should deal with MRSA, 12C**

BOX. Measures for preventing staphylococcal skin infections among sports participants

- Cover all wounds. If a wound cannot be covered adequately, consider excluding players with potentially infectious skin lesions from practice or competitions until the lesions are healed or can be covered adequately.
- Encourage good hygiene, including showering and washing with soap after all practices and competitions.
- Ensure availability of adequate soap and hot water.
- Discourage sharing of towels and personal items (e.g., clothing or equipment).
- Establish routine cleaning schedules for shared equipment.
- Train athletes and coaches in first aid for wounds and recognition of wounds that are potentially infected.
- Encourage athletes to report skin lesions to coaches and encourage coaches to assess athletes regularly for skin lesions.

Thank you